Tab 2 – Daily Schedules

Course Overview
Study Group Assignments
Full Schedule
Model Daily Schedule
Daily Topics Index

Overview

A full schedule of the Institute follows the Study Group information below. In addition, **Tabs A-K** separate the lectures and their associated readings by day. Besides listing the lectures and Faculty, we are providing reprints of required readings, as well as all suggested additional readings that were available at the time of production.

Study Groups

Except as noted we will divide into five Study Groups on a daily basis to discuss the themes, lectures and readings as well as to work on our individual RCT proposals. Please note to which study group you have been assigned, and in which room you will be meeting.

Group 1
Amy Ai
Rebecca Costello
Katherine Hartmann
Carolyn McCarty
Patricia Parker
John Todaro
Mary Zachary
Week 1 Faculty: Abeles, Powell
Week 2 Faculty: Catellier, Davidson
Location: West Room

Group 2
Laura Hinkle Bachmann
Katrina Donahue
Said Ibrahim
Ann McGrath
Joseph Starkey
Maria Trent
Week 1 Faculty: Kaufmann, Willis
Week 2 Faculty: Abeles, Wittes
Location: South Room

Group 3
Amber Barnato
Sonia Duffy
Susmita Kashikar-Zuck
Wendy Nembhard
Daichi Shimbo
Michael Villanueva
Week 1 Faculty: Davidson
Week 2 Faculty: Kaufmann, Gorman
Location: North Room

Group 4
Bryan Blissmer
Carmen Guerra
Fuzhong Li
David Newman-Toker
Jamie Studts
Sandra Waters
Week 1 Faculty: Chaplin, Spring
Week 2 Faculty: Gerin, Tobin
Location: Studio Room

Group 5
Gary Burkholder
Terryl Hartman
B. Alex Matthews
Wendy Nilsen
Janet Thomas
Julie Wetherall
Week 1 Faculty: Mendes de Leon, Keefe
Week 2 Faculty: Proschan
Location:
7/21 – 22 Garden Room
7/23 – 8/1 Old Post

Group Assignments

Please consider the following questions, as they relate to the 8-page proposal you are in the process of developing, to be discussed in your afternoon study group sessions. In addition, to help you develop your 8-page proposal, Dr. Gerin has provided a weighting system concerning the different elements of the proposal. This guide should be used by applicants, to help you apportion your effort where it will be most heavily weighted; and by the reviewers, to provide a guideline to help you evaluate proposals. Note that some elements are weighted differently than they would be in the final version of the proposals. This is partly because some aspects of the proposal will not be presented at the Summer Institute until later in the program (for example, power analysis and sample size).

Monday, July 21

- What design do you plan to use in your study?
- What treatment arms, what control groups will you use?
- Why did you select that particular control group? How, specifically, will use of your control conditions help you to interpret your data?
- Who is your target population?
- What are your study hypotheses? What specific predictions do you make?
- What clinical outcomes are you considering? Are you planning to incorporate measures of putative mechanisms, or mediators, into your design?

Tuesday, July 22

- What do you know about the reliability and validity of the measures you have selected?
- How confident are you that the measures you have selected are appropriate for your particular target population? Have they been validated on that population? What do you do if they haven't?
- Does your design allow you to make causal inferences concerning the predictor variables and the outcomes?
- Write down various possible outcomes of your study (i.e., there is an effect in your experimental but not your control arm; there is an effect in both arms; there is an effect in your experimental arm that goes in the direction opposite to the one you predicted); how do you interpret these various configurations?
- Write down the "best" pattern of results that might occur. Under these ideal conditions, what is the strongest statement you can make about the relationships you have observed?
- What threats to internal and external validity might exist in your design?

Wednesday, July 23

- Why did you select your particular population? Why do you think a funding agency will be enthusiastic about testing the population you have selected?
- What inclusion/exclusion criteria do you plan to use? How can such criteria provide a threat to the external validity of your study?
- To what populations will the results of your study allow you to generalize?

Thursday, July 24

- Which aspects of your protocol might your research participants tend to not adhere to? How do you plan to ensure that research participants in your trial will adhere to the protocol?
- What are the effects on your data of poor adherence to protocol? Discuss this in terms of Type I and Type II error.
- How can you re-design your study to address threats to validity due to poor adherence?

Friday, July 25

- What strategies do you plan to use to recruit your research participants?
- What strategies do you plan to use to improve your recruitment?
- What unanticipated factors might slow down recruitment, or lead to poor retention?
- Come up with a detailed plan that shows reasonable percentages you can expect to see based on your screening criteria, multiplied by the base rates for relevant variables, such as disease prevalence.

Monday, July 28

- Compute sample sizes for your study, based on 80% power and 90% power.
- Why might you use a higher or lower power when estimating sample size?
- What effect size do you plan to look for in your primary outcome? Why not a larger or smaller effect size?
- What are the probable outcomes if you fail to recruit your full sample, as determined by the power analysis?
- What early stopping rules might a DSMB impose on your study?
- What are the advantages to conducting an efficacy study vs. an effectiveness study? What might you learn from each?

Tuesday, July 29

- Develop a budget for your proposal. Justify the "ceiling" limit (e.g., $50,000? $500,000).
- What are the budgetary ceilings of various NIH grant mechanisms?
- Develop a timeline that might be included in your proposal. What activities should the timeline include? How much time do you plan to allow for setup (at the beginning of the grant)? For data analysis (at the end of the funding period)?
- What covariates might you include in your design? How do you plan to measure them?
- What effect does the inclusion of covariates have on your power estimates?

Wednesday, July 30

- Does your design allow you to identify potential mediators?
- What data analyses would you have to conduct to make statements concerning mediation?
- What effects might missing data have on your interpretations of the data?
- What techniques might you use to deal with a missing data problem?
- How might missing data affect the external validity of your study?
- What would be the effect of having missing data on your sample size and power?

Summer Institute Course Schedule

(Subject to Change)

Sunday July 20:

3:00 – 6:30 p.m.	**Arrivals & Registration**	**Foxes Den, Main Bldg.**
6:30 – 7:30 p.m.	**Reception/Dinner**	**Airlie Room, Main Bldg.**
7:30 – 8:30 p.m.	**Welcome and Introduction**	**East Room, Main Bldg.**

Ronald Abeles, Ph.D.
Special Assistant to the Office of the Director
Behavioral & Social Sciences Research
National Institutes of Health

Peter Kaufmann, Ph.D.
Leader, Behavioral Medicine Research Group
National Heart, Lung, and Blood Institute

Karina Davidson, Ph.D.
Director of Clinical Research
Integrative & Behavioral Cardiology
Mount Sinai School of Medicine

Monday July 21:

8:00 a.m. – 9:00 a.m.	**Breakfast**	**All Meals will be held in the Airlie Room, Main Bldg. (except dinner, 7/31)**
9:00 a.m. – 10:00 a.m	**Basic Study Design** **Presentations will be held**	**All** **in the East Room, Main Bldg.**

Carlos Mendes de Leon, Ph.D.
Associate Professor, Medicine & Preventive Medicine
Associate Director of the Section of Community Epidemiologic Research
Department of Medicine
Rush-Presbyterian-St. Luke's Medical

This session will cover the basic design elements of a clinical trial, with particular emphasis on aspects that are relevant for studies of behavioral interventions. A brief overview will be offered of the following topics: basic designs of randomized clinical trials (RCT), selection of experimental and control groups, definition of target population, randomization, blinding, follow-up, and intention-to-treat analysis.

Suggested Reading:

Meinert CL, Tonascia S. Essential design features of a controlled clinical trial. In Meinert CL, Tonascia S. (eds). *Clinical Trials. Design, Conduct, and Analysis* pp. 65-70. New York, NY: Oxford University Press, 1986.

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **A Selected History of Behavioral Randomized Clinical Trials and What We Have Learned**

Lynda Powell, Ph.D.
Professor of Preventive Medicine and Psychology
Department of Preventive Medicine
Rush-Presbyterian-St. Luke's Medical Center

This session will review the most critical elements of behavioral randomized clinical trial design and then provide a critique of selected efficacy trials in the field of cardiovascular disease. These trials will be examined from the point of view of unexpected things that happened that were at odds with the assumptions of basic trial design. It will conclude with a summary of what we have learned and recommendations for ways to strengthen the designs of randomized behavioral clinical trials in the future.

Suggested Readings:

Frasure-Smith N, Prince R. Long-term follow-up of the Ischemic Heart Disease Life Stress Monitoring Program. *Psychosom Med 1989*;51:485-513.

Powell LH. Unanswered questions in the Ischemic Heart Disease Life Stress Monitoring Program (Editorial). *Psychosom Med 1989*;51:479-484.

Writing Committee for the ENRICHD Investigators. The Effects of Treating Depression and Low Perceived Social Support on Clinical Events After Myocardial Infarction: The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. *JAMA, 2003*; 289:3106-3116.

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Hypothesis specification: Including Primary, Secondary and End Points**

Carlos Mendes de Leon, Ph.D.

In this session we will discuss the process that leads to the formulation of the primary study questions. This process involves a consideration of the background literature, clinical challenges in a particular disease-domain, and the potential impact on the overall health of the public. Further discussion will focus on the distinction between primary and secondary aims, as well as selection of primary and secondary endpoints. We will also briefly review the notion of mediating aims. At the end, we will link the specification of primary study aims with the basic design elements of the study.

Suggested Readings:

Goodman SN. Towards evidence-based medical statistics: 1: The P value fallacy. *Annals of Internal Medicine*, 1999, 130: 995-1004.

Rothman KJ, Greenland S. Causation and Causal Inference. In Rothman KJ, Greenland S. (Eds.). *Modern Epidemiology, 2nd Edition*. pp. 7-28. Philadelphia, PA: Lippincott-Raven Publ., 1998.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**
Please see Study Groups for Rooms Assignments

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

Tuesday, July 21

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Measurement, Part 1 – Contemporary Psychometric Perspectives on the Measurement of Behavioral Constructs**

William Chaplin, Ph.D.
Associate Professor
Department of Psychology
St. John's University

In this session we will begin with an overview of the importance of measurement in science and some of the difficulties inherent in the measurement of behavioral constructs. We will then review the classic views of measurement, including reliability, validity, scaling, test

construction, and scoring. We will then consider how these views have evolved during the past 20 years to provide an integration of these classic concepts. Included will be overviews of generalizability theory, decision theory, item response theory, and confirmatory factor analysis in the development and evaluation of behavioral measures.

Required Reading:

John, O.P., Benet-Martinez, V. Measurement: Reliability, Construct Validation and Scale Construction. In Reas HT, Judd, CM. (Eds.). *Handbook of Research Methods in Social and Personality Psychology,* pp.339-369. Cambridge, MA. Cambridge University Press, 2000.

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Measurement Part 2: Applications of Psychometric Theory to Research Design, Statistical Analysis, and the Selection/Development of Measures**

William Chaplin, Ph.D.

The second session on measurement will focus on the application of the theories, concepts and techniques discussed in the first session to the design of clinical trials, the interpretation of the results they generate, and the evaluation of trials conducted by others. In particular attention will be paid to the effect of different populations on the characteristics of measures, the impact that poor measurement has on statistical analyses, and the practical issues that impose limitations on the measures we use. The impact of using few measures, limited ("short") measures, or inadequately developed/evaluated measures on our results and interpretations will be emphasized.

Suggested Reading:

Meyer, G. J., Finn, S. E., Eyde, L. D., Kay, G. G., Moreland, K. L., Dies, R. R., Eisman, E. J., Kubiszyn, T. W., & Reed, G. M. (2001). Psychological testing and psychological assessment: A review of evidence and issues. *American Psychologist*, 56, 128-165.

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **External and Internal Validity**

Karina Davidson, Ph.D.
Director of Clinical Research
Integrative & Behavioral Cardiology
Mount Sinai School of Medicine

In this session we will discuss the degree to which the chosen design establishes the cause-and-effect relationship between the treatment and observed outcome and establishes the

absence of a relationship implies an absence of a cause-and-effect relationship. So to judge the internal validity for each possible design we will answer the following questions:
– Does it rule out alternative explanations?
– Will it convince intervention protagonists that the treatment isn't the active ingredient?
We will then review the relative paucity of information for external validity issues in typical RCT design textbooks, and introduce the RE-AIM framework for judging the external validity of a trial.

Required Reading:

Slack, M.K. & Drugalis, J.R., Establishing the Internal and External Validity of Experimental Studies. *American Journal of Health-Systems Pharm., 2001,* 58: 2173-2184.

Glasgow, R.E., Vogt, T.M., & Boles, S.M. Evaluating the public health impact of health promotion interventions: The RE-AIM framework. *American Journal of Public Health*, 1999, 89: 1322-1327.

Suggested Reading:

Miklowitz, D.J., Clarkin, J.F. Balancing internal and external validity. *Prevention & Treatment*, 1999, 2 (http://www.journals.apa.org/prevention/ volume2/toc-mar21-99.html)

Persons, J.B. & Silberschatz, G. Are results of randomized controlled trials useful to psychotherapists? *Journal of Consulting and Clinical Psychology*, 1998, 66: 126-135.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

7:30 p.m. – 8:30 p.m. **Optional Evening Lecture: Managing your Career**
Full Faculty

Wednesday, July 23

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Defining and Selecting Participants: Eligibility, Inclusion/Exclusion**

Sherry Willis, Ph.D.
Professor of Human Development
The Pennsylvannia State University

This session will cover issues related to defining and selecting the study population, including the need to define the population in advance of the study and the need to state unambiguously inclusion (eligibility) and exclusion criteria. We will discuss the impact of defining the study population on: Study design, ability to generalize, and participant recruitment.

Required Reading:

Textbook, Ch 3

Suggested Reading:

Jobe, J. B., Smith, K., Tennstedt, S. L., Marsiske, M., Willis, S. L., Rebok, G. W., Morris, J. N., Helmers, K., Leveck, M. D., Kleinman, K. (2001). ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled Clinical Trials*, 4, 453-479

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Control Groups, Blindness/Masking, Behavioral "Placebo"**

Francis Keefe, Ph.D.
Professor of Psychiatry and Behavioral Sciences
Professor and Associate Director for Research
Pain & Palliative Care Initiative
Duke University Medical Center
Professor of Psychology: Social & Health Sciences
Duke University

This presentation will focus on issues of control groups, blinding, and masking. Methods and issues in the use of behavioral placebos will also be discussed.

Required Readings:
Textbook, Chapter 6

Hrobjartsson, A. and Gotzsche, P.C. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *NEJM*, 2001, 344: 1594-1602

Turner, J.A., et al., The importance of placebo effects in pain treatment and research, *JAMA*, 1994, 271: 1609-1614.

Suggested Readings:
Beecher, H.K., The powerful placebo, *JAMA*, 1955, 27: 1602-1606

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Data Mangement & Quality Control**

Carlos Mendes de Leon, Ph.D.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

7:30 p.m. – 8:30 p.m. **Optional Evening Lecture: Emerging Topics**

Full Faculty

Thursday, July 24

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Treatment Adherence by Participants**

Sherry Willis, Ph.D.

In this session we will discuss the following topics: Brief review of findings on adherence in clinical trials; Procedures for enhancing adherence; and Monitoring adherence to study regimens.

Required Reading:

Textbook, Ch 9 and 13

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Selecting Treatments & Maintaining Fidelity**

Bonnie Spring, Ph.D.
Department of Psychology
University of Illinois, Chicago

Required Readings:
Textbook, Chapter 10

Suggested Readings:
Bellg, A.J, Borerelli, B, et al., Best Practices for Treatment Fidelity, In Press – *Health Psychology.*

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Case Study**

Francis Keefe, Ph.D.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

Friday, July 25

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Linking Hypotheses, Outcomes & Assesment Measures**

Bonnie Spring, Ph.D., ABPP

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Top Ten Tips for Sucessful Recruitment & Retention**

Lynda Powell, Ph.D.

Required Readings:

Textbook:
Chapter 9: Recruitment of Study Participants, pp. 140-155.
Chapter 13: Patient Adherence, pp 204-222.

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Issues in Behavioral RCTs**

Peter Kaufmann, Ph.D.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 6:30 p.m. **Unscheduled Time**

6:30 p.m. – 7:30 p.m. **Dinner**

Saturday, July 26
Faculty arrivals and departures

Recreation: optional trips to Shanandoah National Park, Luray Caverns, Shanandoah Valley, etc.

Sunday, July 27

Faculty arrivals and departures

Recreation: optional trips to Shanandoah National Park, Luray Caverns, Shanandoah Valley, etc.

7:30 p.m. – 8:30 p.m. **Optional Evening Lecture: Grantsmanship, Part One**

Ronald Abeles, Ph.D.

These two presentations will provide overviews of award mechanisms, review process, and of resources available to applicants. Practical hints on how to prepare a sucessful application will be sprinkled throughout the presentations. The first presentation will concentrate on understanding the NIH and its various opportunities for research and training grants. The second presentation will emphasize the process of preparing a grant application.

Monday, July 28

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Sample Size Determination**

Diane Catellier, Dr.PH
Research Assistant Professor
Deptartment of Biostatistics
University of North Carolina

Determination of the correct sample size and power are important aspects of study planning. This lecture describes factors necessary in all sample size computations and provides useful "approximate" sample-size formulas to aid to investigators in planning research studies to ensure efficient use of resources. Commercial and "freeware" software packages for power analysis increasingly use exact methods when they exist. A series of examples illustrate the use of formulas and commercial software for commonly used study designs in behavioral research. The limitations of the approximate calculator-friendly formulas relative to commercial software are highlighted. Finally, strategies to minimize the sample size through modification of the study design or the use of analytic techniques to increase the efficiency with which information is obtained from a given number of subjects are presented.

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m**. Safety First – The Structure and Function of Data Safety Monitoring Boards (DSMBS)**

Jonathan Tobin, M.D.
President & CEO
Clinical Directors Network

- The problems of multiple comparisons: Power and Confidence
- Establishing Early Stopping Rules
- Early Stopping Rules for Harm
- Early Stopping Rules for Benefit
- Cases and Examples

- Discussion, Questions & Answers

Required Readings:

Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. *Federal Register* Document 12065 (April 18, 1979), http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm

HIPAA Privacy Rule and Its Impact on Research, *Frequently Asked Questions*

NIH Policy for Data and Safety Monitoring (June 10, 1998), *NIH Guide*, Notice 98-084, http://grants.nih.gov/grants/guide/notice-files/not98-084.html

Establishing Data and Safety Monitoring Boards (DSMBS) and Observational Study Monitoring Boards (OSMBS), *National Heart, Lung, and Blood Institute – National Institutes of Health*, (Revised October 30, 2001), http://www.nhlbi.nih.gov/funding/policies/dsmb_est.htm

NIMH Policy on Data and Safety Monitoring in Clinical Trials (September 2002), http://www.nimh.nih.gov/research/safetymonitoring.cfm

Stuart Pocock (1982) Montioring Trial Progress, Chapter 10, *Clinical Trials: A Practical Approach,* (NY: John Wiley & Sons)

Recommended Readings:

Please review additional Federal Register articles and case studies for additonal recommended readings. Case studies will be discussed briefly in the presentation.

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Effectiveness v. Efficacy**

Jack Gorman, Ph.D.
Interim Chair, Dept. of Psychiatry
Mount Sinai School of Medicine

The standard by which treatments are judged is the randomized, blinded, placebo-controlled clinical trial. In general, such trials include rigorous subject selection that includes numerous inclusion and exclusion criteria. Treatment in an efficacy trial is highly restricted to the specific therapies under scientific consideration and is also generally relatively short-term. This method yields the best policy evidence for the usefulness of a treatment when given alone for a specific diagnosis. It has often been noted, however, that few patients actually fit the mold defined by clinical trial entry criteria and that few clinicians practice in the way

prescribed by the trial protocol. Hence, efficacy trials are said to lack ecological or "real world" validity. This has led to widespread advocacy for effectiveness trials that are intended to better mimic conditions under which ordinary patients receive standard care. In effectiveness trials, entry criteria are kept to a minimum, placebo control is usually not used, and treatment protocols are relatively flexible, including the allowance of non-protocol medication. The drawback of such studies is that the resulting data may be difficult, or in some instances, impossible to interpret in a clinically meaningful way. It has been said that a combination of both efficacy and effectiveness trials would be ideal to study the true usefulness of a putative treatment, but this is rarely done in practice, in part because FDA does not require it for registration trials.

Suggested Readings:

Seligman MEP: Afterword—A Plea in PE Nathan and JM Gorman Treatments That Work, *New York: Oxford University Press*, 1998, pp. 568-573

Zimmerman M, Mattia JI, Posternak MA: Are subjects in pharmacological treatment trials of depression representative of patients in routine clinical practice? *American Journal of Psychiatry 2002*;159:469-473

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

7:30 p.m. – 8:30 p.m. **Optional Evening Lecture: Grantsmanship, Part Two**

Ronald Abeles, Ph.D.

These two presentations will provide overviews of award mechanisms, review process, and of resources available to applicants. Practical hints on how to prepare a sucessful application will be sprinkled throughout the presentations. The first presentation will concentrate on understanding the NIH and its various opportunities for research and training grants. The second presentation will emphasize the process of preparing a grant application.

Tuesday, July 29

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Case Study: RCT Dissection**

Jack Gorman, Ph.D.

In psychiatry, there has been a debate about the relative merits of psychotherapy and medication for the treatment of mood and anxiety disorders ever since psychopharmacology for these disorders became possible in the early 1960's. My colleagues and I designed a four site study to test the relative benefits of medication and a type of psychotherapy called cognitive behavioral therapy (CBT) for the treatment of panic disorder. Both the design and implementation of this study forced us to face many of the conflicts between two opposing groups and, most important, to resolve them. We believe that we were successful in designing a trial that was free from "allegiance bias," and that the process of getting to that point is instructive about psychotherapy-psychopharmacology comparison trials in particular and about the design of RCTs in general.

Suggested Readings:

Barlow DH, Gorman JM, Shear MK, Woods SW: Cognitive-behavioral, imipramine, or their combination for panic disorder: a randomized controlled trial. *JAMA 2000*;283:2529-2536

Gorman JM, Barlow DH, Ray S, Shear K, Woods S: Merging the cognitive behavioral and psychopharmacological paradigms in comparative studies: Controversies, issues, and some solutions. *Psychopharmacology Bulletin 2001*;35:111-124

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Power & Money – Relating Sample Size Estimates to Budgets & Workplans**
Jonathan Tobin, M.D.

- Sample Size Calculations:
- Effect Size
- Variance
- Type I Errors: Level of Significance (Alpha)
- Type II Errors: Power (1-Beta)
- Statistical Power Analysis
- Theory
- Demonstrations
- Developing Workplans and Timelines
- Developing Staffing Plan
- Budgeting using Excel
- Cases and Examples
- Discussion, Questions & Answers

Recommended Readings:

NIH PHS398 Form,
http://grants1.nih.gov/grants/funding/phs398section_1.html#4_detailed

Initial Budget Period – Direct Costs Only Form,
http://grants1.nih.gov/grants/funding/phs398/fp4.rtf

Entire Budget Period – Direct Costs Only Form,
http://grants1.nih.gov/grants/funding/phs398/fp5.rtf

Salary Maximum Information available at: http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-03-034.html

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Modeling/Adjustments for Covariats**

Michael A. Proschan, Ph.D.
Mathematical Statistician
Office of Biostatistics Research
National Heart, Lung, and Blood Institute

This session covers the two main advantages of covariate adjustment—reduction of variance and correction for baseline imbalances— in trials with a continuous outcome. Covariate adjustment in dichotomous outcome trials using logistic regression is also discussed, as is subgroup analysis.

Required Readings:

Textbook, chapter 16;

Price and Sikora (1995). *Treatment of Cancer*, 3rd edition, Chapman and Hall, London, section 52.4

ISIS-2 Collaborative Group (1988). *The Lancet* 2, 349-360.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

7:30 p.m. – 8:30 p.m. **Evening Lecture: Meta-Analysis & Integrating Across RCTs**

Janet Wittes, Ph.D.

Required Readings:

Peto, R., Why do we need systematic overviews of randomized trials? Stat Med, 1987. 6: p. 233-240.

Bailey, K., Inter-study differences: how should they influence the interpretation and analysis of results? *Stat Med, 1987*. 6: p. 351-358.

Cook, D.J., et al., Should unpublished data be included in meta-analysis? Current convictions and controversies. *Journal American Med Assn*, 1993. 269: p. 2749-2753.

Suggested Readings:

Dickersin, K. and J.A. Berlin, Meta-analysis: state-of-the-science. *Epidemiologic Reviews, 1992*. 14: p. 154-176.

Fleiss, J.L., The statistical basis of meta-analysis. *Statistical Methods in Medical Research, 1993*. 2(2): p. 121-146.

Follmann D, Proschan M, *Biometrics 55*, 732-737 (1999).

Oakes, M., The logic and role of meta-analysis in clinical research. *Statistical Methods in Medical Research*, 1993. 2(2): p. 147-160.

Wednesday, July 30

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 10:00 a.m **Survival Analysis**

Michael Proschan, Ph.D.

Sometimes the outcome in behavioral trials is time to an event such as a heart attack or alcohol relapse. This session covers the fundamentals of analyzing such data, including the Kaplan-Meier survival curve, the logrank test to compare survival curves, and the Cox proportional hazards model to compare survival curves while adjusting for baseline covariates.

Required Readings:

Textbook, chapter 14

10:00 a.m. – 10:20 a.m. **Discussion and Questions**

10:20 a.m. – 10:30 a.m. **Morning Break**

10:30 a.m. – 11:30 a.m. **Analysis of Mediating Variables in Behavioral Intervention Research**

Diane Catellier, Dr.PH

This lecture describes statistical methods that provide information about how interventions achieve their effects. Behavioral interventions are typically based on theories of behavior change (i.e., conceptual model) whereby intervention components are selected based on their ability to change the outcome measure of interest. For example, mediators targeted by an intervention to decrease sedentary behavior might include access to physical activity opportunities and self-efficacy or competence in engaging in physical activity. The intervention is designed to change mediators, which are hypothesized to be causally related to the outcome measure. Mediation analysis is the methodology to test these effects. As the field of behavioral research matures, mediation analysis will play an increasingly important role in testing the validity of theories of behavior change leading to more effective interventions. Major topics to be discussed include: (1) substantive examples of mediation analysis, (2) statistical methods to assess mediation, (3) related statistical methods.

11:30 a.m. – 11:50 a.m. **Discussion and Questions**

11:50 a.m. – 1:00 p.m. **Lunch**

1:00 p.m. – 2:00 p.m. **Missing Data**

Janet Wittes, Ph.D.
President
Statistics Collaborative, Inc.

The validity of inference from randomized clinical trials arises from the act of randomization and the fidelity of the statistical analysis to the randomized groups. When all data on the endpoints are available, statistically rigorous analysis is conceptually easy to perform. When, however, some randomized participants lack measurement of the endpoint, the approach to analysis becomes problematic. If the unavailable data are missing purely at random, then the analysis may proceed simply by using the available data. Unfortunately, in trials of behavioral interventions, the fact of having a missing endpoint is rarely a result of a purely random process. Instead, the missingness may be related to a characteristic of the participant, or, even worse, to a property of the intervention itself. This talk discusses a number of approaches to dealing with missing data - encouraging participants to complete the trial, redefining the endpoint so that the fact of missingness becomes part of the definition of the endpoint, and structuring the statistical analysis to reduce the bias induced by missing data. The effect on sample size and attenuation of estimated effect size will be discussed.

2:00 p.m. – 2:20 p.m. **Discussion and Questions**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

2:30 p.m. – 4:00 p.m. **Group Activities (e.g., case studies, group assignments)**

4:00 p.m. – 5:30 p.m. **Unscheduled Time**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 7:30 p.m. **Dinner**

Thursday, July 31

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 4:00 p.m. **Reports of Student Work Groups: Designing Clinical Trials**
Drs. Abeles, Davidson & Kaufmann

10:20 a.m. – 10:30 a.m. **Morning Break**

11:50 a.m. – 1:00 p.m. **Lunch**

2:20 p.m. – 2:30 p.m. **Afternoon Break**

5:30 p.m. – 6:30 p.m. **Voluntary 30 Minute Individual Consultations**

6:30 p.m. – 8:00 p.m. **Graduation Dinner and Ceremony** **Pavilion, Formal Gardens**

Friday, Aug 1

8:00 a.m. – 9:00 a.m. **Breakfast**

9:00 a.m. – 2:30 p.m. **Reports of Student Work Groups: Designing Clinical Trials**
Drs. Abeles, Davidson & Kaufmann

10:20 a.m. – 10:30 a.m. **Morning Break**

11:50 a.m. – 1:00 p.m. **Lunch**

2:30 p.m. – 3:00 p.m. **Check-out**

Model Day

The following is offered as a sample organization of a day. Changes are probable!

Time	Activity
8:00—9:00 AM	Breakfast
9:00 - 10:00 AM	Lecture 1
10:00 – 10:20 AM	Discussion and Questions
10:20 – 10:30 AM	Refreshment Break
10:30 – 11:30 AM	Lecture 2
11:30 – 11:50 AM	Discussion and Questions
11:50 – 1:00 PM	Lunch
1:00 PM – 2:00 PM	Lecture 3
2:00 – 2:20 PM	Discussion and Questions
2:20 – 2:30 PM	Refreshment Break
2:30 – 4:00 PM	Group Activities (e.g., case studies, group assignments/tasks)
4:00 – 5:30 PM	Unscheduled time for reading, recreation
5:30 – 6:30 PM Mon – Thurs ONLY	Voluntary Individual Consultation Opportunities
6:30-7:30 PM	Dinner
7:30-8:30 PM	Occasional, optional discussions or lectures

Daily Topics Index

A. *Sunday, July 20*
Welcome – Abeles, Davidson, Kaufmann

B. *Monday, July 21*
Basic Study Design – Mendes de Leon
History of RCTs – Powell
Hypothesis Specification – Mendes de Leon

C. *Tuesday, July 22*
Measurement, Part 1 – Chaplin
Measurement, Part 2 – Chaplin
External & Internal Validity – Davidson
Optional Evening Lecture, Managing Your Career – Full Faculty

D. *Wednesday, July 23*
Defining & Selecting Participants – Willis
Control Groups – Keefe
Data & Quality – Mendes de Leon
Optional Evening Lecture, Emerging Topics – Full Faculty

E. *Thursday, July 24*
Treatment Adherence – Willis
Selecting Treatments – Spring
Case Study – Keefe

F. *Friday, July 25*
Linking – Spring
Recruitment & Retention – Powell
Issues in Behavioral RCTs – Kaufmann

G. *Saturday & Sunday, July 26 & 27*
Optional Recreation
Sunday Optional Evening Lecture, Grantsmanship Part 1 – Abeles

H. *Monday, July 28*
Sample Size Determination – Catellier
DSMBs – Tobin
Effectiveness v. Efficacy – Gorman
Optional Evening Lecture, Grantsmanship Part 2 – Abeles

I. *Tuesday, July 29*
Case Study: RCT Dissection – Gorman
Sample Size & Budgets – Tobin
Modeling/Covariate Adjustments – Proschan
Evening Lecture – Meta-Analysis & Integration – Wittes

J. *Wednesday, July 30*
Survival Analysis – Proschan
Mediating Variables – Catellier
Missing Data – Wittes

K. *Thursday & Friday, July 31 & August 1*
Student Work Group Reports
Thursday Evening Graduation Ceremony and Cook-Out
Student Work Group Reports
Friday Afternoon Check-Out